

Cell Biology

RADIOTHERAPY OF GLIOBLASTOMA MULTIFORME

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Abstract

The purpose of our research is to develop improved therapeutic treatments for glioblastoma multiforme (GBM). GBM is an aggressive and deadly form of brain cancer. Patients diagnosed with GBM normally have life expectancies of less than a year even with aggressive treatments that include surgery, radiotherapy, and chemotherapy. The infiltrative growth pattern of GBM prevents complete surgical removal. Therefore, recurrence rates are very high even after therapy.

Current radiotherapy uses high doses of radiation to kill GBM cells remaining after surgery but high doses of radiation can damage normal brain tissue. We propose to specifically target GBM tumor cell nuclei using Hoechst 33342 which binds to the minor groove of DNA. Targeted cells will be specifically irradiated by a neutron capture reaction in Gd-Hoechst 33342 and by ¹²⁵I-Hoechst 33342 decay. Two GBM cell lines (U87 and U251) and the third cell line, Chinese hamster ovary (CHO) cells, were used for these studies.

The clonogenic responses of CHO, U251, and U87 cells to neutron and γ irradiation were determined. Addition of feeder cells and glutamine improved U87 and U251 cell plating efficiency. In all cases, a significantly lower neutron dose was required to kill the cells with the GBM cells being particularly sensitive to neutrons.

Any modification in the radiation response due to Hoechst 33342 alone was first investigated. CHO cells were treated with 0 μ M, 5 μ M, 10 μ M, 20 μ M, and 50 μ M Hoechst 33342 for 30 minutes at 37°C and then γ irradiated. We find Hoechst 33342 slightly radioprotects the cells so it can be a good vector to use to transport radioactivity to the cell nucleus. ¹²⁵I-Hoechst 33342 clonogenic assays are currently in progress.

Targeting GBM cells with radioactively tagged Hoechst 33342 should spare normal brain tissue and improve the patients' survival.